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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,660	12/08/2000	Haruhiko Kouhara	038602/1023	1711

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/21/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/731,660

Applicant(s)

KOUHARA ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,4-6,11-13 and 20-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,4-6,11-13 and 20-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/24/2003 has been entered.

Applicants amendment of claims 4 and 11 and the addition of new of claims 20-23, Paper No. 10, 10/23/2002, is acknowledged. Claims 2, 4-6, 11-13 and 20-23 are at issue and are present for examination. Applicants arguments presented on 6/24/2003, Paper No. 15, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

Applicants amendment of the first page of the specification to indicate that "This application is a divisional of U.S. Serial No. 08/980,523, filed December 1, 1997, now U.S. Patent No. 6,310,181 which is incorporated by reference in its entirety (including any drawings), and claims priority to U.S. Provisional Application 60/032,093" is acknowledged. It is suggested that this be further amended to "...claims priority to U.S.

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Provisional Application No. 60/032,093, filed December 12, 1996", although this may be done by informal examiners amendment at the time of allowance.

Applicants request that the specification be amended as such above at the time of allowance is acknowledged.

Claim Objections

Claim 21 is objected to because of the following informalities:

Claim 21 recites "...of any one of said second polypeptides." There is insufficient antecedent basis for "said second polypeptides" and it is suggested that this be amended to "said second proteins".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 11-13 and 20-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is stated in the previous office action as it applied to claims 2, 4-6 and 11-13.

In response to this rejection applicants have amended claim 11© to recite that the FRS2 polypeptide has FRS2 activity. This argument is not found persuasive

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because as stated in the previous office action, applicants teach that FRS2 stands for Fibroblast Growth Factor Receptor Protein Kinase Substrate 2" and the FRS2 protein/polypeptide preferably has a number of different biological activities (i.e. the ability to regulate growth factor stimulation of cellular differentiation and cellular proliferation by linking stimulated fibroblast growth factor receptor (FGFR) to the Ras/MAPK cascade via the Grb-2/Sos complex and Grb-2 binding activity). The recitation remains indefinite in that while applicants state in the specification they prefer the "FRS2 polypeptide " to have a number of functional activities, it remains unclear which of these preferred functional activities are necessary limitations of a "FRS2 polypeptide".

Claim 11 (claims 2, 12-13 and 20-21 and 23 dependent on) remains indefinite in the following : Part (k) recites "the complement of..." It is believed that applicants intent was "is the complement of..." . This rejection was stated in the previous office action. In response to this rejection applicants state that claim 11 has been amended as previously indicated, however, while applicants amended claim 11 parts (f) and (i), applicants failed to amend part (k) and said nothing regarding this remaining part of the previous 112 second paragraph rejection.

Claim 22 is indefinite in that it is unclear and confusing in the recitation "The nucleic acid probe of claim 1,..." as claim 1 has now been cancelled was not previously drawn to a nucleic acid probe, but rather a nucleic acid . For the purpose of advancing prosecution the claim is interpreted as if it depended from claim 4.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4-6 11-13 and 20-23 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office actions, Paper No. 8, 4/23/2002, Paper No. 11, 1/24/2003, as it applied to claims 2, 4-6 and 11-13. Applicants have traversed the rejection in Paper No. 10, 10/23/2002 and Paper No. 13, 5/14/2003. Applicants have now amended claims 4 and 11 and added new claims 20-23 and traverse the rejection as it applies to the amended claims.

Applicants traverse this rejection on the basis applicants amendments of claims 4 and 11 have corrected the insufficiencies of the claims such that the rejection should be reconsidered and withdrawn. Specifically, applicants submit that claim 4 has been amended such the referred to "structural limitation" now refers to the claimed nucleic acid probe and not to the probe's target as was the situation previously. Applicants argument is not found persuasive. While applicants submission is acknowledged claim 4 remains rejected for a lack of written description. In spite of applicants amendment, applicants have not adequately described the genus of nucleic acid probes comprising a

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nucleotide sequence that encodes a polypeptide comprising a mere 10 contiguous amino acids of SEQ ID NO: 1.

Applicants submit that applicants amendment of claim 11(d) to recite "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, but not all of the following segments of amino acid residues: 1-10, 11-152, or 153-508." has overcome the current rejection. Applicants argument is not found persuasive. Applicants attention is further drawn to claim 11 part (h), which is analogous to previous claim 11 (d) with the exception that part (h) does not require that the encoded polypeptide be a FRS2 polypeptide and rather then requiring that it has the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one of the following segments of amino acid residues: 1-10, 11-152, or 153-508, it requires that it has the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one or more of the domains selected from the group consisting of a myristylation region, a phosphotyrosine binding region and a C-terminal region. The only difference between previous part (d) and current part (h) is that part (h) does not specifically describe each of the regions which may be lacking by amino acid position, but rather by the name of the domain as described in the specification. Each of these domains refers to the same portion of SEQ ID NO: 1 as the amino acid sequences described in part (d). Thus the claim continues to read on any nucleic acid molecule which encodes any polypeptide.

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As stated in the previous office action, applicants specification only provides a single representative species which encodes the FRS2 polypeptide having the amino acid sequence of SEQ ID NO: 1, encompassed by the claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these nucleic acids by any identifying structural or functional characteristics. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 2, 4-6, 11-13 and 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a FRS2 polypeptide, wherein said FRS2 polypeptide has the amino acid sequence of SEQ ID NO: 1, does not reasonably provide enablement for any nucleic acid encoding any FRS2 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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The rejection is stated in the previous office actions, Paper No. 8, 4/23/2002, Paper No. 11, 1/24/2003, as it applied to claims 2, 4-6 and 11-13. Applicants have traversed the rejection in Paper No. 10, 10/23/2002 and Paper No. 13, 5/14/2003. Applicants have now amended claims 4 and 11 and added new claims 20-23 and traverse the rejection as it applies to the amended claims.

Applicants continue to traverse this rejection in a similar fashion as the above rejection on the following basis. Applicants submit that claim 4 has been amended such the referred to "structural limitation" now refers to the claimed nucleic acid probe and not to the probe's target as was the situation previously. Applicants further submit that applicants specification (page 12, line 11 through page 13, line 8) describes nucleic acid probes and that one of ordinary skill in the art knows that nucleic acid probes can be used to detect the presence or absence of nucleic acid molecules in various applications such as diagnostic methods. In response to this assertion applicants are asked what specific "use" would one of ordinary skill in the art know that the nucleic acid probes of claim 4 can be used for. Can all of the encompassed nucleic acid probes of claim 4 be used for such a use or are there additional uses that some of the encompassed nucleic acid probes might be used for that others might not be used for? And once again what is this specific use?

With respect to claim 11 part (d) applicants argue as above that claim 11 (d) has been amended such that it recites "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, **but not all** of the following segments of amino acid residues: 1-10, 11-152, or

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153-508." And that this has overcome the current rejection. Applicants further submit that the specification provides sufficient disclosure to enable a person of ordinary skill in the art to make and use the nucleic acid molecule of the present invention. While applicants disclosure does teach how to make and use some of the nucleic acid molecules encompassed by the current claims, applicants disclosure does not teach how to make and use the full scope of the genus of nucleic acid molecules encompassed by the current claims. See especially those nucleic acid molecules encompassed by claim 11 part (h), as discussed above, which requires that the encoded polypeptide comprises the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1, except that it lacks at least one or more of the domains selected from the group consisting of a myristylation region, a phosphotyrosine binding region and a C-terminal region. Thus this portion of the claim, like previously amended part (d) encompasses any nucleic acid which encodes any polypeptide.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any nucleic acid encoding any polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 11 remains rejected under 35 U.S.C. 102(b) as being anticipated by Otilie et al. (Oncogene Vol 7, No 8: 1625-1630, August 1992).

The rejection is stated in the previous office actions as it applied to claims 4 and 11. In response to this rejection applicants have amended claims 4 and 11 and traverse the rejection as it applies to the amended claims.

Applicants amendment and traversal of the rejection of claim 4 is persuasive.

Applicants submit that Otilie et al. does not satisfy any of the requirements of claim 11. Applicants submit that the based on previous Blast alignments, Otilie et al. does not share 90% sequence identity to the amino acid sequence of SEQ ID NO: 1 as stated in part (c) of claim 11 and applicants amendment of part (d) of claim 11 as discussed above, requires that at least one of the recited segments of amino acid residues be present. As discussed above, while Otilie et al. may not teach a nucleic acid molecule as encompassed by parts (c) and (d) of claim 11, the taught nucleic acid molecule of Otilie et al. is encompassed by part (h) of claim 11. Claim 11 continues to encompass any possible nucleic acid which encodes any polypeptide (See above

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discussion of claim 11 part (h) under 112 first paragraph rejections). Thus, Otilie et al. continues to anticipate claim 11.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2 and 11-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Oncogene, Vol 13, pages 721-729, 1996).

The rejection is stated in the previous office action as it applied to claims 1, 3, 4 and 11.

The rejection is stated in the previous office actions, Paper No. 8, 4/23/2002, Paper No. 11, 1/24/2003, as it applied to claims 2, 4-6 and 11-13. Applicants have traversed the rejection in Paper No. 10, 10/23/2002 and Paper No. 13, 5/14/2003. Applicants have now amended claims 4 and 11 and added new claims 20-23 and traverse the rejection as it applies to the amended claims.

Applicants amendment and traversal with respect to claim 4 has caused the withdrawal of claims 4-6.

Applicants further traverse this rejection on the basis that Wang et al. fails to disclose any sequences for the SNT-like proteins discussed in the paper and it is the

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examiner's burden to provide evidence to support that the claimed sequence shares sequence identity or homology with the prior art sequence. Absent such evidence, applicants maintain that the claimed invention is not obvious over Wang et al. and applicants present Exhibit A, Xu et al., to support their position.

Applicants argument is not found persuasive because as stated and discussed above under the 112 first paragraph rejections, claim 11 part (h) encompasses an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1, except that it lacks at least one or more of the domains selected from the group consisting of a myristylation region, a phosphotyrosine binding region and a C-terminal region, which is thus equivalent to any nucleic acid molecule which encodes any polypeptide. Thus the specific sequence of a nucleic acid molecule is unnecessary to make obvious the claim, as any nucleic acid sequence of the claim encompasses any nucleic acid sequence which encompasses any polypeptide. As previously stated, one of ordinary skill in the art at the time of filing would have been motivated to isolate and clone a nucleic acid encoding the SLP proteins taught by Wang et al. in order to express these SLP proteins recombinantly so that there role in signal transduction and their involvement with the known oncogene ras. The referred to nucleic acid encodes a SLP protein, hence it is encompassed by those nucleic acid molecules of claim 11 and made obvious by Wang et al.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgH